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**UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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1314.1058-00

EXAMINER

FORMAN, B

ART UNIT	PAPER NUMBER
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1685

DATE MAILED: 11/20/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/523,066

Applicant(s)

TULLY ET AL.

Examiner

BJ Forman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- 1) ☒ Responsive to communication(s) filed on 12 July 2000.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above claim(s) 1-10 and 16-23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 11-15 and 24-26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some * c) ☐ None of the CERTIFIED copies of the priority documents have been:
1. ☐ received.
2. ☐ received in Application No. (Series Code / Serial Number) _____.
3. ☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5.
- 18) ☐ Interview Summary (PTO-413) Paper No(s) _____.
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-10 and 16-23, drawn to a method of identifying a gene or genes in non-human animals, classified in class 424, subclass 9.1.

II. Claims 11-15 and 24-26, drawn to a method of identifying a gene or genes in *Drosophila*, classified in class 424, subclass 9.1.

2. The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are unrelated methods. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions the inventions are not disclosed as capable of use together and they have different modes of operation and different functions i.e. the method of Invention I operates by training non-human animals and extracting brain-specific RNA for analysis and function to identify non-human gene or genes and the method of Invention II operates by training *Drosophila* and extracting head tissue-specific RNA for analysis and functions to identify a *Drosophila* gene or genes.

3. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

4. During a telephone conversation with Richard Wagner on 17 October a provisional election was made with traverse to prosecute the invention of Group II, claims 11-15 and 24-26. Affirmation of this election must be made by applicant in replying to this Office action.

Claims 1-10 and 16-23 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

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5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Priority

6. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. The Provisional Application filed 10 March 1999 upon which priority is claimed provides adequate support under 35 U.S.C. 112 for claims 11-15 and 24-26 of this application.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 11-15 and 24-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 11-15 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete in Claim 11 for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the steps reciting "conditions appropriate" for training *Drosophila* to induce transcription-dependent memory and the steps reciting "condition insufficient" for training *Drosophila* to induce transcription-dependent

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memory. It is suggested that Claim 11 be amended to recite the missing steps (Specification, page 10, lines 2-21).

b. Claims 11-15 are indefinite in Claim 11 (c) and (f) (iii) for the recitations "synthesizing DNA probes using the RNA extracted...) because it is unclear how the RNA is used to synthesize the probes. It is suggested that Claim 11 (c) and (f) (iii) be amended to clarify e.g. replace "DNA" with "cDNA" and to replace "using" with "complementary to" (see specification page 11, lines 5-6).

c. Claims 11-15 are indefinite in Claim 11 (d) and (f) (iv) for the recitations "exposing" because "exposing" is a non-specific term and therefore it is unclear how the DNA probe are exposed. The Claims are further indefinite in Claim 11 (d) and (f) (iv) for the recitations "conditions appropriate for hybridization" because "hybridization" lacks proper antecedent basis in the step of "exposing". It is suggested that Claim 11 (d) and (f) (iv) be amended to clarify i.e. replace "exposing" with "hybridizing".

d. Claims 11-15 are indefinite in Claim 11 (d) and (f) (iv) for the recitations "wherein a signal is produced" because "signal" lacks proper antecedent basis in the probe of (c) and (f) (iii). It is suggested that Claim 11 (c) and (f) (iii) be amended to provide proper antecedent basis for the signal e.g. insert "labeled" before "DNA" and that Claim 11 (d) and (f) (iv) be amended to properly depend from Claim 11 (c) and (f) (iii) e.g. insert "from said labeled probe" after "produced".

e. Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the steps reciting "conditions sufficient to induce transcription-independent memory but not transcription-dependent memory. It is suggested that Claim 14 be amended to recite the missing steps (specification, page 10, lines 2-21).

f. Claims 24-26 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete in Claim 24 for omitting essential steps, such omission amounting to a gap between -

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the steps. See MPEP § 2172.01. The omitted steps are: the steps reciting "conditions appropriate" for training *Drosophila* to induce transcription-dependent. It is suggested that Claim 24 be amended to recite the missing steps (Specification, page 10, lines 2-21).

g. Claims 24-26 are indefinite in Claim 24 (c) and (f) (iii) for the recitations "synthesizing DNA probes using the RNA extracted...) because it is unclear how the RNA is used to synthesize the probes. It is suggested that Claim 24 (c) and (f) (iii) be amended to clarify e.g. replace "DNA" with "cDNA" and to replace "using" with "complementary to" (see specification page 11, lines 5-6).

h. Claims 24-26 are indefinite in Claim 24 (d) and (f) (iv) for the recitations "exposing" because "exposing" is a non-specific term and therefore it is unclear how the DNA probes are exposed. The claim is further indefinite in (d) and (f) (iv) for the recitations "under conditions appropriate for hybridization to the DNA probes to complementary DNA sequences on the microarray chips" because it is unclear what "conditions are being claimed and because it is unclear whether hybridization occurs. It is suggested that Claim 24 (d) and (f) (iv) be amended to clarify i.e. replace "exposing" with "hybridizing" and to delete "under conditions appropriate for hybridization to the DNA probes to complementary DNA sequences on the microarray chips".

i. Claims 24-26 are indefinite in Claim 24 (d) and (f) (iv) for the recitations "wherein a signal is produced" because "signal" lacks proper antecedent basis in the probe of (c) and (f) (iii). It is suggested that Claim 24 (c) and (f) (iii) be amended to provide proper antecedent basis for the signal e.g. insert "labeled" before "DNA" and that Claim 24 (d) and (f) (iv) be amended to properly depend from Claim 24 (c) and (f) (iii) e.g. insert "from said labeled probe" after "produced".

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. Claims 11-15 and 24-26 are rejected under 35 U.S.C. 103(a) as being obvious over Yin et al. (Cell, 1994, 79: 49-58) in view of Tully et al. (U.S. Patent No. 5,929,223, filed 7 October 1994) and Luo et al. (Society for Neuroscience Abstracts, 1999, 25(1-2): 2164)

Regarding Claim 11, Yin et al. teach a method of identifying a gene involved in transcription-dependent memory comprising: training *Drosophila* to induce transcription-dependent memory formation in said *Drosophila* i.e. spaced training, (page 50, last paragraph—page 51-first paragraph); extracting RNA from head tissue of said trained *Drosophila*; exposing the RNA to DNA sequences from a gene of the *Drosophila* genome i.e. dCREB2-b cDNA, under conditions appropriate for hybridization wherein a signal is produced upon hybridization and detecting the signal produced (page 56, last paragraph) and performing a statistical comparison between the signal detected and a signal detected in a control (page 51, left column, last line-right column, first paragraph). Yin et al. teach training control *Drosophila* under conditions insufficient to induce transcription-dependent memory i.e. massed training (page 55, right column, second full paragraph) and performing statistical comparisons between the trained *Drosophila*. Yin et al. also teach a comparison of hybridization signals between *Drosophila* trained to induce transcription-dependent memory and *Drosophila* trained insufficiently to induce transcription dependent memory i.e. in the absence of training (page 50, last paragraph and Fig. 1). Yin et al. do not teach synthesizing DNA probes from the extracted RNA and exposing the DNA probes to microarray chips containing DNA sequences from genes of the *Drosophila* genome. However, Yin et al. teach

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that the cAMP signal transduction pathway is critically involved with memory events and the pathway involves numerous cAMP response genes including transcription factors and they teach that drugs that interfere with transcription or translation disrupt memory. These teachings suggest that memory events require de novo gene expression and that numerous genes are involved with the memory events (page 79, left column, last paragraph-right column first full paragraph). Additionally, Luo et al. teach a method similar to Yin et al. of identifying a gene or genes involved in memory, wherein following training, RNA is extracted and exposed to DNA probes on a microarray chip to thereby identify a gene or genes involved in memory and they teach the microarray is a powerful method of analyzing a expression in complex process such as memory (page 2164, Abstract No. 864.9). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Yin et al. with the teachings Yin et al. and Luo et al. to obtain the claimed invention because the skilled practitioner in the art would have been motivated with a reasonable expectation of success to modify the gene identification of Yin et al. with the microarray identification of Luo et al. wherein multiple genes involved in the complex process of memory are identified the for the expected benefit of simplifying the identification of Yin et al. by eliminating the complex and time consuming process of creating transgenic *Drosophila* to thereby identify a single gene and for the additional benefit of economy of time and labor by replacing multiple single-gene identifications with the microarray identification taught by Luo et al. for the identification numerous genes involved in transcription-dependent memory suggested by Yin et al. and Luo et al. The skilled practitioner in the art would have been further motivated to modify the mRNA analysis of Yin et al. with reverse transcribed cDNA for the known benefits of DNAs increased stability.

Regarding Claim 12, Yin et al. teach the method wherein transcription-dependent memory formation is long term memory formation (page 49, last paragraph-page 50, right column first full paragraph).

Regarding Claim 13, Yin et al. teach the method wherein transcription-dependent memory formation is induced using a spaced training protocol (page 50, last paragraph-page 51, first paragraph. Additionally, Yin et al. teach the conditions of a massed training protocol (page 55, right column, first full paragraph, lines 24-29). Yin et al. do not teach the method wherein the hybridization signals from the spaced trained and massed trained *Drosophila* are compared. However, Tully et al. teach a similar method comprising: training two groups of *Drosophila*, one under conditions to induce transcription-dependent memory and a second under condition insufficient to induce transcription-dependent memory, extracting RNA from head tissue of both groups, hybridizing the RNA to DNA sequences from genes of the *Drosophila* and comparing the hybridization signals between the two groups (Column 25, lines 6-30). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Yin et al. with the teaching of Tully et al. to obtain the claimed invention because the skilled practitioner in the art would have been motivated with a reasonable expectation of success to modify the RNA analysis of Yin et al. wherein hybridization signals from trained and untrained *Drosophila* are compared to further compare hybridization signals from *Drosophila* following the different training protocols as taught by Tully et al. for the obvious benefit of analyzing training-specific expression to thereby identify memory-specific expression.

Regarding Claim 14, Yin et al. teach the conditions sufficient to induce transcription-independent memory formation but not transcription-dependent memory formation i.e. massed training (page 55, right column, first full paragraph, lines 24-29).

Regarding Claim 15, Yin et al. teach transcription-independent memory formation is induced using a massed training protocol (page 55, right column, first full paragraph, lines 24-29).

Regarding Claim 24, Yin et al. teach a method of identifying a gene involved in transcription-dependent memory comprising: training *Drosophila* to induce transcription-

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dependent memory formation in said *Drosophila* i.e. spaced training, (page 50, last paragraph—page 51-first paragraph); extracting RNA from head tissue of said trained *Drosophila*; exposing the RNA to DNA sequences from a gene of the *Drosophila* genome i.e. dCREB2-b cDNA, under conditions appropriate for hybridization wherein a signal is produced upon hybridization, detecting the signal produced, comparing the signal to the signal from control *Drosophila* (page 56, last paragraph) and performing a statistical comparison between the signal detected and a signal detected in a control (page 51, left column, last line-right column, first paragraph). Yin et al. do not teach synthesizing DNA probes from the extracted RNA and hybridizing the DNA probes to microarray chips containing DNA sequences from the genes of the *Drosophila* genome. However, Yin et al. teach that the cAMP signal transduction pathway is critically involved with memory events and the pathway involves numerous cAMP response genes including transcription factors and they teach that drugs that interfere with transcription or translation disrupt memory. These teachings suggest that memory events require de novo gene expression and that numerous genes are involved with the memory events (page 79, left column, last paragraph-right column first full paragraph). Additionally, Luo et al. teach a similar method of identifying a gene or genes involved in memory comprising: training, extracting RNA from head tissue and exposing the RNA to microarray chips containing DNA sequences of the genome (page 2164, Abstract No. 864.9). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Yin et al. with the teachings of Luo et al. to obtain the claimed invention because the skilled practitioner in the art would have been motivated with a reasonable expectation of success to modify the gene identification of Yin et al. with the microarray identification of Luo et al. wherein multiple genes involved in the complex process of memory are identified for the expected benefit of simplifying the identification of Yin et al. by eliminating the complex and time consuming process of creating transgenic *Drosophila* to thereby identify a single gene and for the additional benefit of economy of time and labor by replacing multiple single-gene

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identifications with the microarray identification taught by Luo et al. for the identification numerous genes involved in transcription-dependent memory suggested by Yin et al. and Luo et al. The skilled practitioner in the art would have been further motivated to modify the mRNA analysis of Yin et al. with reverse transcribed cDNA for the known benefits of DNAs increased stability.

Regarding Claim 25, Yin et al. teach the method wherein said transcription-dependent memory formation is long term memory formation i.e. spaced training (page 51, left column, first paragraph).

Regarding Claim 26, Yin et al. teach the method wherein said transcription-dependent memory formation is induced using a spaced training protocol (page 51, left column, first paragraph).

Conclusion

11. No claim is allowed.
12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:45 TO 4:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.

November 16, 2000

S. E. Forman